

CLAIMS

We claim:

- 5 95. An immunoglobulin comprising a protection protein in association with an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain.
- 10 96. The immunoglobulin of claim 95 further comprising an immunoglobulin derived light chain having at least a portion of an antigen binding domain associated with said immunoglobulin derived heavy chain.
- 15 97. The immunoglobulin of claim 95 further comprising a second immunoglobulin derived heavy chain having at least a portion of an antigen binding domain associated with said protection protein.
- 20 98. The immunoglobulin of claim 97 further comprising at least one immunoglobulin derived light chain having at least a portion of an antigen binding domain bound to said second immunoglobulin derived heavy chain.
- 25 99. The immunoglobulin of claim 95 further comprising an immunoglobulin J chain bound to said immunoglobulin derived heavy chain and optionally to a second immunoglobulin derived heavy chain.
100. The immunoglobulin of claim 95 that is a therapeutic immunoglobulin.
- 30 101. The immunoglobulin of claim 100 wherein said therapeutic immunoglobulin binds to mucosal pathogen antigens.
102. The immunoglobulin of claim 101 that is capable of preventing dental caries.

103. The immunoglobulin of claim 95 wherein said antigen binding domain is capable of binding an antigen from S. mutans serotypes c, e and f or S. sobrinus serotypes d and g.

5 104. The immunoglobulin of claim 95 wherein said protection protein has an amino acid sequence which substantially corresponds to at least a portion of the amino acid residues selected from the group consisting of 1 to 627 and 1 to 606 of the rabbit polyimmunoglobulin  
10 receptor and wherein said protection protein does not have an amino acid residue sequence corresponding to amino acid residues 628-755 of the rabbit polyimmuno-  
globulin receptor.

15 105. The immunoglobulin of claim 104 wherein said protection protein has an amino acid sequence which does not contain amino acid residues corresponding to amino acid residues 628 to 775 of the rabbit polyimmunoglobulin receptor and which does contain amino acid residues which correspond to one or more of the following amino acid  
20 segments:

- a) amino acids corresponding to amino acid residues 21-43 of the rabbit polyimmunoglobulin receptor;
- b) amino acids corresponding to amino acid residues 1 - 118 of the rabbit polyimmunoglobulin receptor;
- 25 c) amino acids corresponding to amino acid residues 119 - 223 of the rabbit polyimmunoglobulin receptor;
- d) amino acids corresponding to amino acid residues 224 - 332 of the rabbit polyimmunoglobulin receptor;
- e) amino acids corresponding to amino acid residues 333 - 441 of the rabbit polyimmunoglobulin receptor;
- 30 f) amino acids corresponding to amino acid residues 442 - 552 of the rabbit polyimmunoglobulin receptor;

g) amino acids corresponding to amino acid residues 553 - 606 or 553 - 627 of the rabbit polyimmunoglobulin receptor.

5 106. The immunoglobulin of claim 95 wherein said protection protein has an amino acid sequence which does not contain amino acid residues of a polyimmunoglobulin receptor of a species which are analogous to amino acid residues 628 to 755 of the rabbit polyimmunoglobulin receptor and which does contain amino acid residues from  
10 a polyimmunoglobulin receptor of a species which are analogous to one or more of the following amino acid segments:

a) amino acids corresponding to amino acid residues 21 - 43 of the rabbit polyimmunoglobulin receptor;

15 b) amino acids corresponding to amino acid residues 1 - 118 of the rabbit polyimmunoglobulin receptor;

c) amino acids corresponding to amino acid residues 119 - 223 of the rabbit polyimmunoglobulin receptor;

20 d) amino acids corresponding to amino acid residues 224 - 332 of the rabbit polyimmunoglobulin receptor;

e) amino acids corresponding to amino acid residues 333 - 441 of the rabbit polyimmunoglobulin receptor;

25 f) amino acids corresponding to amino acid residues 442 - 552 of the rabbit polyimmunoglobulin receptor;

g) amino acids corresponding to amino acid residues 553 - 606 or 553 - 627 of the rabbit polyimmunoglobulin receptor.

30 107. The immunoglobulin of claim 106 wherein said species is human.

108. The immunoglobulin of claim 95 wherein said protection protein includes the amino acid sequence of at least one of the domains selected from the group consist-

ing of the following portions of the rabbit polyimmuno-  
globulin receptor: domain I, domain II, domain III,  
domain IV, domain V, and amino acid residues 553 to 627  
of domain VI; and does not have an amino acid sequence  
5 corresponding to amino acid residues 628-755 of the  
rabbit polyimmunoglobulin receptor.

109. The immunoglobulin of claim 95 wherein said  
protection protein does not have any amino acid sequence  
which corresponds to or is analogous to amino acid resi-  
10 dues 628-755 of the rabbit polyimmunoglobulin receptor  
and which does include:

a) at least one domain which is from the  
polyimmunoglobulin receptor of a first animal and which  
is analogous to at least a portion of the following amino  
15 acid segments of the rabbit polyimmunoglobulin receptor:  
domain I, domain II, domain III, domain IV, domain V, and  
amino acid residues 553 to 627 of domain VI;

b) at least one domain which is from the  
polyimmunoglobulin receptor of a second animal and which  
20 corresponds to or is analogous to the following amino  
acid residue segments of the rabbit polyimmunoglobulin  
receptor: domain I, domain II, domain III, domain IV,  
domain V, and amino acid residues 553 to 627 of domain  
VI.

25 110. The immunoglobulin of claim 95 wherein said  
protection protein does not have any amino acid sequence  
which corresponds to or is analogous to amino acid resi-  
dues 628-755 of the rabbit polyimmunoglobulin receptor  
and which does include:

30 a) at least one amino acid segment which is from  
the polyimmunoglobulin receptor of a first animal and  
which is analogous to at least a portion of the following  
amino acid residue segments of the rabbit

polyimmunoglobulin receptor: domain I, domain II, domain III, domain IV, domain V, and amino acid residues 553 to 627 of domain VI;

b) at least one amino acid segment which is from the polyimmunoglobulin receptor of a second animal and which corresponds to or is analogous to the following amino acid residue segments of the rabbit polyimmunoglobulin receptor: domain I, domain II, domain III, domain IV, domain V, and amino acid residues 553 to 627 of domain VI.

111. The immunoglobulin of claim 110 wherein said first animal is a mammal and said second animal is a rabbit.

112. The immunoglobulin of claim 110 wherein said first animal is a human and said second animal is a rabbit.

113. The immunoglobulin of claim 95 wherein said immunoglobulin derived heavy chain contains at least a portion of an IgM or IgA heavy chain of any subtype.

114. The immunoglobulin of claim 95 wherein said immunoglobulin derived heavy chain is comprised of immunoglobulin domains from two different isotopes of immunoglobulin.

115. The immunoglobulin of claim 115 wherein said immunoglobulin domains are selected from the group consisting of:

a) the C<sub>H</sub>1 of a mouse IgG1 and the C<sub>H</sub>2 and C<sub>H</sub>3 of mouse IgA; and

b) the C<sub>H</sub>1 and C<sub>H</sub>2 of a mouse IgG1 and the C<sub>H</sub>2 and C<sub>H</sub>3 of mouse IgA;

116. The immunoglobulin of claim 95 wherein said antigen binding domain substantially corresponds to the Guy's 13 heavy chain variable region.

117. The immunoglobulin of claim 96 wherein said antigen binding domain substantially corresponds to the Guy's 13 light chain variable region.

118. A composition comprising the immunoglobulin of any of claims 95-117 and at least one plant macromolecule.

119. The composition of claim 118 wherein said plant macromolecule is derived from a dicotyledonous, monocotyledonous, solanaceous, alfalfa or tobacco plant.

120. The composition of claim 118 wherein said plant macromolecule is selected from the group consisting of ribulose biphosphate carboxylase, light harvesting complex, pigments, secondary metabolites and chlorophyll.

121. The composition of claim 118 wherein said immunoglobulin is present in a concentration of between 0.001% and 99% mass excluding water.

122. The composition of claim 119 wherein said plant macromolecules are present in a concentration of between 1% and 99% mass excluding water.

123. A method of producing the immunoglobulin of any of claims 95-117 comprising the steps of:

(a) introducing into a plant cell an expression vector containing a nucleotide sequence encoding a protection protein operably linked to a transcriptional promoter; and

(b) introducing into said plant cell an expression vector containing a nucleotide sequence encoding an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain operably linked to a transcriptional promoter.

124. The method of claim 123 further comprising the step of:

(c) introducing into said plant cell an expression vector containing a nucleotide sequence encoding an immunoglobulin derived light chain having at least a portion of an antigen binding domain operably linked to a transcriptional promoter.

5 125. The method of claim 123 further comprising the step of introducing into said plant cell an expression vector containing a nucleotide sequence encoding an immunoglobulin J chain operably linked to a transcriptional promoter.

10 126. The method of claim 123 wherein said immunoglobulin derived heavy chain is immunoglobulin alpha chain and said immunoglobulin derived light chain is an immunoglobulin kappa or lambda chain.

15 127. The method of claim 123 wherein said immunoglobulin derived heavy chain is comprised of portions of immunoglobulin alpha chain and immunoglobulin gamma chain.

20 128. The method of claim 123 wherein said plant cells are part of a plant.

129. The method of claim 123 further comprising growing said plant cells into a regenerated plant.

25 130. The method of claims 128 or 129 wherein said plant is a dicotyledonous, monocotyledonous, solanaceous, leguminous, alfalfa or tobacco plant.

131. The method of claim 123 wherein said immunoglobulin derived heavy chain is a chimeric immunoglobulin heavy chain.

30 132. A method of producing a therapeutic immunoglobulin composition containing plant macromolecules, said method comprising the step of shearing under pressure plants or parts thereof to produce a pulp containing a therapeutic immunoglobulin and plant macro-

molecule mixture, said immunoglobulin comprising a protection protein, and wherein said immunoglobulin is encoded by at least one nucleic acid sequence that has been introduced into the cells of said plants.

5     ~~133~~. The method of claim 132 further comprising the step of separating said solid plant derived material from said liquid.

10     ~~134~~. The method of claim 132 wherein said portion of said plant is a leaf, stem, root, tuber, fruit or entire plant.

15     ~~135~~. The method of claim 132 wherein said shearing is accomplished by a mechanical device which releases liquid from the apoplast or symplast of said plant.

20     ~~136~~. The method of claim 133 wherein said separation is by centrifugation, settling, flocculation or filtration.

25     ~~137~~. A method for producing an assembled immunoglobulin molecule having heavy, light and J chains and a protection protein comprising the steps of:

30     a) introducing into a eukaryotic cell nucleotide sequences operably linked for expression encoding:

i) an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain,

25     ii) an immunoglobulin derived light chain having at least a portion of an antigen binding domain,

iii) an immunoglobulin J chain, and

iv) a protection protein; and

30     b) maintaining said cell under conditions allowing production and assembly of said immunoglobulin derived heavy and light chains, said immunoglobulin J



chain and said protection protein into an immunoglobulin molecule.

138. A method for producing an assembled immunoglobulin molecule having heavy, light and J chains and a protection protein by maintaining under conditions allowing protein production and immunoglobulin assembly, a eukaryotic cell containing nucleotide sequences operably linked for expression encoding:

- i) an immunoglobulin derived heavy chain having at least a portion of an antigen binding domain,
- ii) an immunoglobulin derived light chain having at least a portion of an antigen binding domain,
- iii) an immunoglobulin J chain, and
- iv) a protection protein.

139. The method of claims 137 or 138 wherein said eukaryotic cell is a plant cell.

140. A method of making an immunoglobulin resistant to environmental conditions comprising the steps of :

- a) operably linking a nucleotide sequence encoding at least a portion of the antigen binding domain derived from an immunoglobulin heavy chain to a nucleotide sequence encoding at least one domain derived from an immunoglobulin alpha heavy chain to form a nucleotide sequence encoding a chimeric immunoglobulin heavy chain;
- b) expressing said nucleotide sequence encoding said chimeric immunoglobulin heavy chain to produce said chimeric immunoglobulin heavy chain in a plant cell which also contains at least one other molecule selected from the group consisting of: a protection protein, an immunoglobulin derived light chain having at least a

portion of an antigen binding domain and an immunoglobulin J chain; and  
thereby allowing the chimeric immunoglobulin heavy chain  
to assemble with said at least one other molecule to form  
5 said immunoglobulin resistant to said environmental  
conditions.

141. The method of claim 140 wherein said other  
molecule is a protection protein and said plant cell also  
contains an immunoglobulin derived light chain having at  
10 least a portion of an antigen binding domain and an  
immunoglobulin J chain.

142. A process for producing an immunoglobulin  
resistant to environmental conditions by maintaining  
under conditions allowing protein production and  
15 immunoglobulin assembly a plant cell containing:

a) a nucleotide sequence encoding a chimeric  
immunoglobulin heavy chain in which a nucleotide sequence  
encoding at least a portion of an antigen binding domain  
derived from heavy chain is operably linked to a  
20 nucleotide sequence encoding at least one domain derived  
from an immunoglobulin alpha heavy chain; and

b) at least one other molecule selected from the  
group consisting of: a protection protein, an immunoglobulin  
derived light chain having at least a portion of  
25 an antigen binding domain and an immunoglobulin J chain;  
thereby allowing the chimeric immunoglobulin heavy chain  
to assemble with said at least one other molecule to form  
said immunoglobulin resistant to said environmental  
conditions.

30 143. The immunoglobulin of claim 95 wherein said  
chimeric immunoglobulin heavy chain contains an immunoglobulin  
domain from one of the following immunoglobulin

heavy chains: IgG, IgA, IgM, IgE, IgD; and also contains a protection protein-binding domain from IgA or IgM.

5     144. The immunoglobulin of claim 143 wherein said immunoglobulin heavy chains are human, rodent, rabbit, bovine, ovine, caprine, fowl, canine, feline or primate immunoglobulin heavy chains.

10     145. The immunoglobulin of claim 143 wherein said protection protein-binding domain is from the IgA of a human, rodent, rabbit, bovine, ovine, canine, feline or primate.

146. The immunoglobulin of claim 143 wherein said chimeric immunoglobulin heavy chain is comprised of immunoglobulin chains of mouse IgG1 and said protection protein-binding domain is from mouse IgA or IgM.

15     147. The immunoglobulin of claim 143 wherein said chimeric immunoglobulin heavy chain is comprised of immunoglobulin domains of a human IgG, IgM, IgD or IgE and said protection protein-binding domain is from a human IgA or IgM.